

The association of waist circumference with ambulatory blood pressure is independent of alternative adiposity indices

Olebogeng H.I. Majane^a, Gavin R. Norton^a, Muzi J. Maseko^a, Siyanda Makaula^a, Nigel Crowther^b, Janice Paiker^b, Lutgarde Thijs^c, Richard Brooksbank^a, Pinhas Sareli^a, Jan A. Staessen^c and Angela J. Woodiwiss^a

Aim The relationship between waist circumference (WC) and conventional blood pressure (BP) is independent of other clinical indices of adiposity. As ambulatory BP may offer more prognostic information than conventional BP, we aimed to identify whether indices of central adiposity are associated with ambulatory BP independent of other indices of adiposity.

Methods The relationship between indices of adiposity [WC, waist-to-hip ratio, body mass index (BMI) or skin-fold thickness] and ambulatory or conventional BP was determined in 300 randomly selected individuals of African descent living in an urban developing community in South Africa. Relationships were determined with multiple indices of adiposity in the same regression model and after adjusting for age, gender, alcohol and tobacco intake, the presence or absence of diabetes mellitus or inappropriate blood glucose control [haemoglobin A_{1c} (HbA_{1c})], antihypertensive therapy and menopausal status.

Results Sixty-five per cent of participants were overweight or obese. With respect to the relationships between indices of adiposity, BMI and WC showed the strongest correlation ($r = 0.84$, $P < 0.0001$). After including all indices of adiposity and confounders in the model, WC was the only clinical index of adiposity which independently predicted 24-h (partial $r = 0.15$, $P < 0.005$) and conventional (partial $r = 0.14$, $P < 0.005$) systolic BP and 24-h (partial $r = 0.13$, $P < 0.02$)

and conventional (partial $r = 0.40$, $P < 0.0001$) diastolic BP. After adjusting for other adiposity indices and confounders, every 1 SD (15 cm) increase in WC resulted in a 4.04 mmHg increase in 24-h systolic BP and a 4.33 mmHg increase in 24-h diastolic BP. Similar results were obtained in the subgroup of 237 participants not receiving antihypertensive therapy.

Conclusion WC is the only clinical index of adiposity that is associated with 24-h and conventional BP independent of other adiposity indices in a community with a high prevalence of obesity. *J Hypertens* 25:1798–1806 © 2007 Lippincott Williams & Wilkins.

Journal of Hypertension 2007, 25:1798–1806

Keywords: ambulatory blood pressure, obesity, waist circumference

^aCardiovascular Pathophysiology and Genomics Research Unit, School of Physiology, ^bDepartment of Chemical Pathology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa and ^cDivision of Hypertension and Cardiovascular Rehabilitation, Department of Cardiovascular Diseases, University of Leuven, Belgium

Correspondence to Angela J. Woodiwiss, Cardiovascular Pathophysiology and Genomics Research Unit, School of Physiology, University of the Witwatersrand Medical School, 7 York Road, Parktown, 2193, Johannesburg, South Africa
Tel: +27 11 717 2363; fax: +27 11 717 2153;
e-mail: angela.woodiwiss@physiology.wits.ac.za

Received 11 October 2006 Revised 3 April 2007

Accepted 10 April 2007

Introduction

The prevalence of obesity is rapidly increasing in both developed [1] and developing [2] countries. There is now substantial evidence from large population-based studies in favour of excess adiposity being a major determinant of blood pressure (BP) and the development of hypertension [3–5]. In this regard, present evidence suggests that waist circumference (WC) appears to be the preferred clinical index when relating adiposity to conventional BP [3–16]; however, to our knowledge studies that have compared the relative impact of indices of central fat and body mass index (BMI) on ambulatory BP have either recruited small study samples, have been non-random, have focused on waist-to-hip ratio rather than WC as the index of central fat, and have produced ambiguous results [17–21]. As 24-h ambulatory BP is a better index of cardiovascular outcomes

[22–25] and target organ effects [26] than conventional BP values, the relative impact of indices of central and general adiposity on ambulatory BP requires elucidation. In the present study we assessed whether any one commonly used clinical index of adiposity (WC, waist-to-hip ratio, BMI and skin-fold thickness) predicts ambulatory BP independent of the others. This study was conducted in a randomly selected population sample, with a high prevalence of obesity, living in an urban developing community in South Africa.

Methods

Study subjects

The protocol of the study was approved by the University of the Witwatersrand Committee for Research in Human Subjects (approval number: M02-04-72). Participants

gave informed, written consent. This study was part of the African Project on Genes in Hypertension. The population sample has recently been described [27]. Since the initial analysis, a larger study sample has been recruited. Briefly, nuclear families were recruited if at least one or two offspring of at least 16 years of age and one or both parents were available for examination. Of 496 South African individuals of African ancestry randomly recruited from metropolitan areas of Johannesburg, 395 had all the required clinical data. Of these, 300 had more than 20 h of ambulatory BP recordings and more than 10 and five readings for the computation of daytime and night-time means, respectively.

Clinical, demographic and anthropometric measurements

A standardized questionnaire was administered to obtain demographic data and information on each participant's medical history, smoking habits, intake of alcohol, use of medication, and menopausal status. Height and weight were measured with the participants standing and wearing indoor clothes with no shoes. BMI was calculated as weight in kilograms divided by the square of height in metres. Waist and hip circumference were measured using a standard approach, and triceps and subscapular skin-fold thickness determined using a skinfold calliper (Harpender skinfold calliper). Skin-fold thickness was reported as the mean of triceps and subscapular values. Subjects were identified as being overweight if their BMI was $\geq 25 \text{ kg/m}^2$ and obese if their BMI was $\geq 30 \text{ kg/m}^2$. Standard laboratory blood tests of renal function, liver function and haematological parameters were performed to ensure that subjects did not have subclinical renal, hepatic or haematological disorders. Diabetes mellitus or inappropriate blood glucose control was defined as the use of insulin or oral hypoglycaemic agents, or a percentage glycated haemoglobin (HbA_{1c}) (Roche Diagnostics, Mannheim, Germany) $>7\%$ [28]. Follicular stimulating hormone (Bayer, Leverkusen, Germany) was measured to confirm menopausal status. To determine 24-h urine Na^+ excretion (an index of Na^+ intake), timed urine samples were obtained over a period of at least 24 h after discarding urine excreted immediately prior to the start of the collection period. Urine Na^+ concentrations were measured and 24-h urine Na^+ excretion rate calculated from the product of urine volume and urine Na^+ concentration. The quality of the urine samples was determined as described previously [29,30].

Conventional blood pressure measurements

Trained observers measured brachial artery BP in a clinic environment using a mercury sphygmomanometer. The conventional BP measurement was obtained on the same day as ambulatory BP monitors were initialized. The participants were seated and asked to rest for 5 min. The observers measured the participants' sitting BP five consecutive times. Systolic and diastolic (phase V)

BP were determined to the nearest 2 mmHg, according to the recommendations of the European Society of Hypertension [31]. In most participants standard cuffs were used, which had an inflatable bladder with a length of 22 cm and a width of 12 cm. If arm circumference exceeded 31 cm, larger cuffs with a $31 \times 15 \text{ cm}$ bladder were employed. The five readings obtained at each of the visits were averaged to obtain a single systolic and diastolic BP value. Hypertension was defined as the use of antihypertensive medication or if the mean of five conventional BP measurements was $\geq 140/90 \text{ mmHg}$ in those not receiving medication.

Ambulatory blood pressure measurements

Twenty-four-hour ambulatory BP monitoring was performed using oscillometric monitors (SpaceLabs, model 90207; SpaceLabs, Redmond, Washington, USA). The size of the cuff was the same as that used for conventional BP measurements. The accuracy of ambulatory monitors was checked monthly against a mercury manometer. If the monitors recorded pressure values that deviated from a mercury reading by more than 4 mmHg, monitors were recalibrated by the commercial suppliers. The monitors were programmed to measure BP at 15-min intervals from 0600 to 2200 h and then at 30-min intervals from 2200 to 0600 h. Participants kept a diary card for the duration of the recordings to note the time of going to bed in the evening and getting up in the morning. From each participant's diary card data we determined the awake and asleep periods. Considering the patterns of daily activities, the daytime and night-time intervals were defined as time intervals ranging from 0900 to 1900 h and from 2300 to 0500 h respectively. These fixed clock-time intervals [32,33] were defined in order to eliminate the transition periods (evening and morning) during which BP changes rapidly in most subjects. Intra-individual means of the ambulatory measurements were weighted by the time interval between successive recordings [32,33]. Ambulatory BP data were expressed as 24-h, daytime and night-time average systolic and diastolic BP. Daytime and night-time periods were defined as described previously [32].

Data analysis

Database management and statistical analyses were performed with SAS software, version 9.1 (SAS Institute Inc., Cary, North Carolina, USA). Data from individual subjects were averaged and expressed as mean \pm SD. Proportions were compared with χ^2 analysis. Linear regression analysis was used to determine relationships. Stepwise regression analysis was performed to determine independent effects of indices of adiposity on BP. Included in the regression model were age, gender, alcohol and tobacco intake (defined as the presence or absence of daily tobacco or alcohol ingestion), postmenopausal status (confirmed with follicle stimulating hormone measurements), the presence or absence of diabetes mellitus or inappropriate blood glucose control (considered as a single

covariate) and the use of antihypertensive therapy (either receiving therapy or not receiving therapy). To identify those indices of adiposity associated with BP independent of other indices of adiposity, indices of adiposity were considered together in the regression model. In addition to including antihypertensive therapy as a covariate in the regression analyses, sensitivity analyses were repeated in a subgroup of subjects who were not receiving antihypertensive therapy ($n = 237$).

Results

Characteristics of the participants

Table 1 gives the demographic and clinical characteristics of the participants. More women than men participated (Table 1). Sixty-five per cent of subjects were overweight or obese, with 27.6% being overweight and 37.7% being obese. In the group 42% were hypertensive, 20% were receiving therapy for hypertension, and 8% had diabetes mellitus (Table 1). A relatively small percentage of the group were smokers (12%), mostly due to lack of affordability and also due to the greater proportion of women (who traditionally do not smoke in this population) compared to men. Twenty-four-hour urine Na^+ excretion rates (an index of Na^+ intake) despite being high, were not associated with indices of obesity (r values: BMI = 0.05; WC = 0.003; skin-fold thickness = 0.003; waist-to-hip ratio = 0.11; $P > 0.1$ for all). The mean age (41.4 ± 17.9 years) and BMI ($28.9 \pm 7.3 \text{ kg/m}^2$) and the percentage of women (63%) in all individuals recruited was the same

as that for participants with all clinical data (Table 1). The demographic and clinical characteristics of the participants with ambulatory BP measurements that met prespecified quality control criteria were similar to those of participants with all clinical data (Table 1). In addition, although they were younger (38.1 ± 16.5 years), fewer individuals had hypertension (26.2%) and there were fewer postmenopausal women (29%), the other demographic and clinical characteristics in the subgroup of subjects not receiving antihypertensive therapy ($n = 237$) did not differ from those of either the participants with ambulatory BP measurements or those with all clinical data (data not shown).

In the present study only 0.76% of visits had fewer than the planned conventional BP recordings. The frequency of identical consecutive conventional BP recordings was 0.25%. The occurrence of conventional BP values recorded as an odd number was 0% and of the 3936 systolic and diastolic conventional BP readings, 27.8% ended on a zero (expected = 20%). Average conventional systolic and diastolic BP values were higher than average 24-h, daytime or night-time systolic and diastolic BP values (Table 1).

Association between indices of adiposity

BMI and WC showed the strongest relationship. The weakest relationship was noted between waist-to-hip ratio and BMI. Furthermore, only a trend effect was noted between waist-to-hip ratio and skin-fold thickness (Table 2). Similar associations were evident in the subgroup of participants who were not receiving antihypertensive therapy (data not shown).

Unadjusted associations between indices of adiposity and blood pressure

BMI, WC, waist-to-hip ratio and skin-fold thickness were all correlated with conventional systolic BP (Fig. 1). BMI, WC and waist-to-hip ratio, but not skin-fold thickness, were correlated with 24-h systolic BP (Fig. 2). Significant correlations between either BMI ($r = 0.35$, $P < 0.0001$), WC ($r = 0.41$, $P < 0.0001$), waist-to-hip ratio ($r = 0.27$, $P < 0.0001$) or skin-fold thickness ($r = 0.25$, $P < 0.0001$) and conventional diastolic BP were also noted before adjustments; whereas BMI ($r = 0.17$, $P = 0.0031$), WC ($r = 0.28$, $P < 0.0001$) and waist-to-hip ratio ($r = 0.23$, $P < 0.0001$), but not skin-fold thickness ($r = 0.09$, $P = 0.14$), were correlated with 24-h diastolic BP. Significant unadjusted correlations were noted between body weight

Table 1 Demographic, anthropometric and clinical characteristics of study subjects

	All participants	Participants with ambulatory BP
Sample number	395	300
% Female	63	63
Age (years)	41.8 ± 18.1	43.0 ± 17.9
Height (m)	161 ± 9	161 ± 9
Weight (kg)	75 ± 19	75 ± 19
BMI (kg/m^2)	28.8 ± 7.4	29.0 ± 7.4
Waist circumference (cm)	89 ± 15	89 ± 15
Hip circumference (cm)	107 ± 15	106 ± 15
WHR	0.84 ± 0.10	0.84 ± 0.10
% Overweight/obese	65	66
Skin-fold thickness (cm)		
Subscapular	2.41 ± 1.37	2.47 ± 1.36
Triceps	1.90 ± 1.20	2.01 ± 1.25
Mean	2.15 ± 1.16	2.24 ± 1.19
Urine Na^+ excretion (mmol/day)	113.9 ± 53.5	110.4 ± 48.1
% smokers	12.2	12.7
% alcohol ^a	21.2	22.3
% with hypertension	42.0	41.7
% treated for hypertension	20.3	21.0
% with DM	8.2	8.1
HbA _{1c} (%)	6.02 ± 1.07	6.04 ± 1.07
n (%) postmenopausal	98 (39)	78 (41)
Clinic SBP/DBP (mm Hg)	$130 \pm 23/84 \pm 12$	$131 \pm 23/84 \pm 12$
Ambulatory BP (mmHg)		
24 h SBP/DBP (mmHg)	—	$119 \pm 16/73 \pm 11$
Daytime SBP/DBP (mmHg)	—	$123 \pm 16/78 \pm 11$
Night-time SBP/DBP (mmHg)	—	$112 \pm 18/65 \pm 12$

BMI, body mass index; BP, blood pressure; DBP, diastolic BP; DM, diabetes mellitus; HbA_{1c}, glycated haemoglobin; SBP, systolic BP; WHR, waist-to-hip ratio.

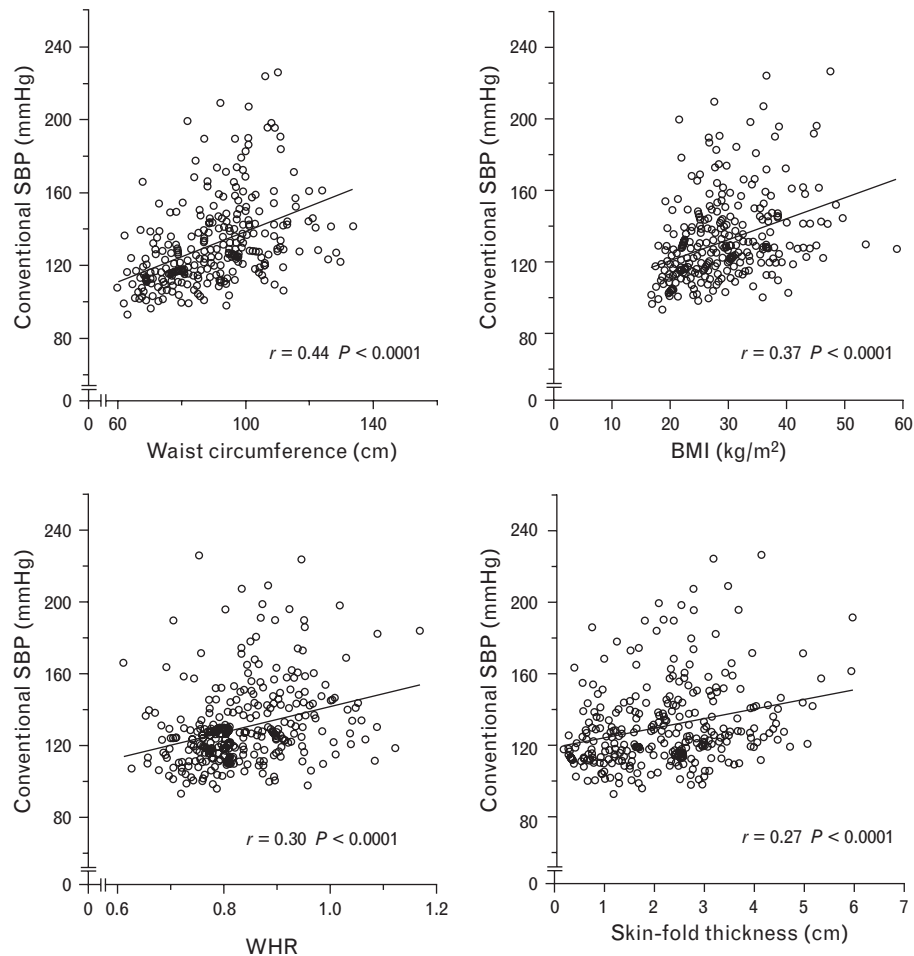
^a Percentage of participants consuming alcohol on a daily basis.

Table 2 Correlation matrix between indices of adiposity in study group ($n = 300$)

	WC (cm)	WHR	Mean skin-fold thickness
Body mass index (kg/m^2)	0.84**	0.18*	0.66**
Waist circumference (WC) (cm)	—	0.58**	0.58**
Waist-to-hip ratio (WHR)	—	—	0.11 [†]

Numbers are correlation coefficients (r). * $P < 0.01$; ** $P < 0.0001$ for the relationships; [†] $P = 0.058$.

Fig. 1



Relationships between indices of adiposity and conventional systolic blood pressure (SBP) in study subjects ($n = 300$). BMI, body mass index; WHR, waist-to-hip ratio.

and conventional BP (SBP: $r = 0.29$, $P < 0.0001$; DBP: $r = 0.32$, $P < 0.0001$), 24-h BP (SBP: $r = 0.20$, $P = 0.0005$; DBP: $r = 0.16$, $P = 0.0052$), daytime BP (SBP: $r = 0.20$, $P = 0.0005$; DBP: $r = 0.15$, $P = 0.011$), and night-time BP (SBP: $r = 0.18$, $P = 0.0016$; DBP: $r = 0.18$, $P = 0.0019$). The unadjusted associations between indices of adiposity and BP in the subgroup of subjects who were not receiving antihypertensive therapy (data not shown) were similar to those in the group of subjects with ambulatory BP.

Conventional and ambulatory blood pressure and indices of adiposity in separate models

When considering indices of adiposity in separate regression models, but adjusting for other confounders, BMI, WC and skin-fold thickness were independent predictors of conventional systolic and diastolic BP, whereas waist-to-hip ratio was only associated with conventional diastolic BP (Table 3). Waist circumference was the only index of adiposity associated with 24-h systolic and diastolic BP after adjustments for other covariates

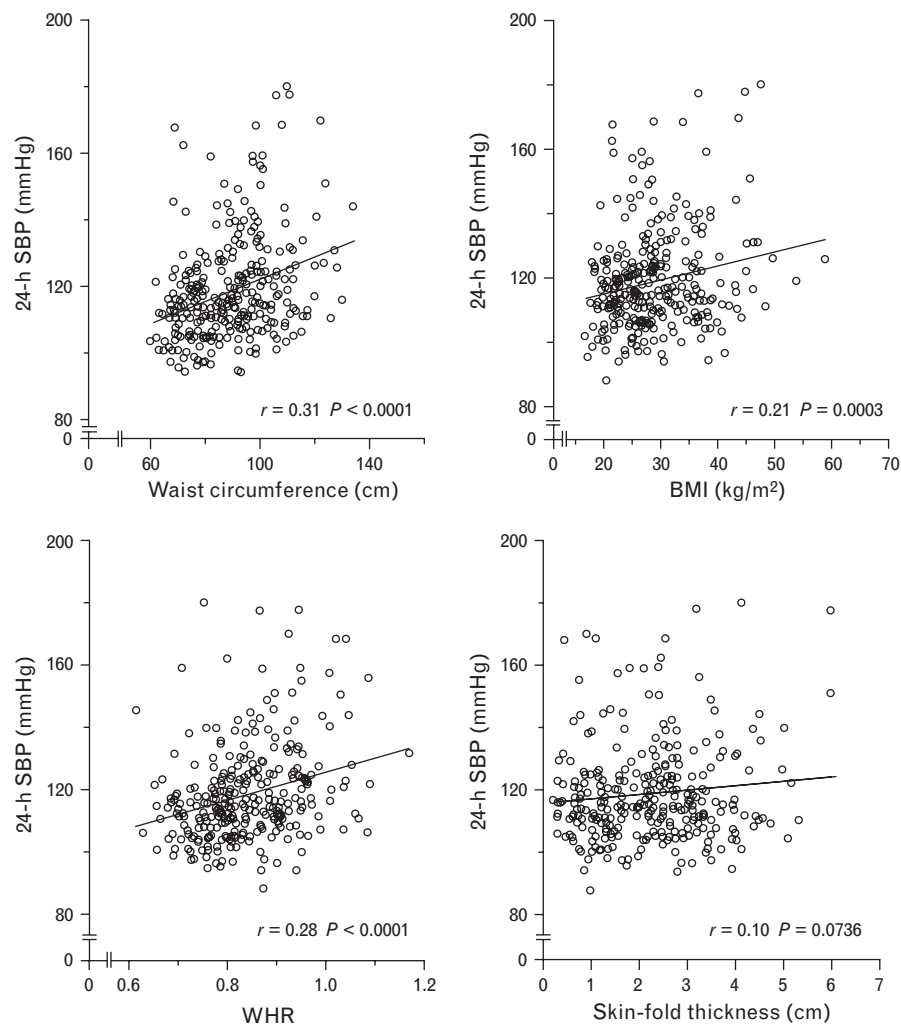
(Table 3). Nevertheless, the relationship between BMI and 24-h systolic BP was close to significant (Table 3). Analyses of daytime and night-time systolic and diastolic BP revealed similar results, with WC being the only index of adiposity associated after adjustments for other covariates (Table 3). Similar results were observed in the subgroup of subjects not receiving antihypertensive therapy (data not shown).

Although body weight was associated with conventional BP (systolic BP: partial $r = 0.10$, $P = 0.03$; diastolic BP: partial $r = 0.21$, $P < 0.0001$), no associations with 24-h, daytime or night-time systolic and diastolic BP were noted after adjustments for other covariates.

Conventional and ambulatory blood pressure and indices of adiposity in the same model

The independent relationship between WC and either conventional or 24-h BP (Table 3) persisted after BMI, waist-to-hip ratio and skin-fold thickness were included in

Fig. 2



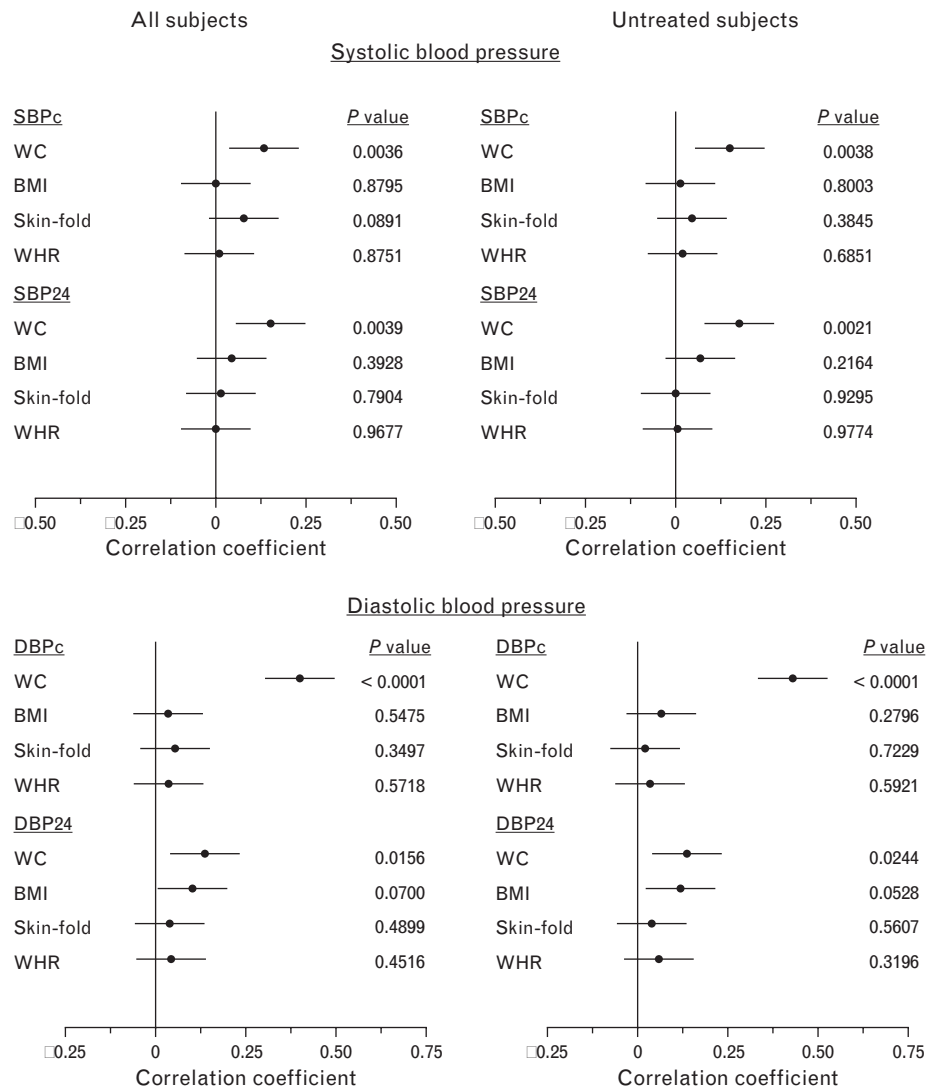
Relationships between indices of adiposity and 24-h ambulatory systolic blood pressure (SBP) in study subjects ($n = 300$). BMI, body mass index; WHR, waist-to-hip ratio.

Table 3 Partial correlation coefficients (r) for the relationship between indices of adiposity considered separately in the regression model and systolic (SBP) or diastolic blood pressure (DBP) in the study group ($n = 300$)

	Partial r^a	P value ^a	Partial r^a	P value ^a	Partial r^a	P value ^a	Partial r^a	P value ^a
	Conventional SBP (mmHg)		24-h SBP (mmHg)		Daytime SBP (mmHg)		Night-time SBP (mmHg)	
Waist circumference (cm)	0.13	<0.005	0.14	0.009	0.14	0.009	0.11	0.031
Body mass index (kg/m ²)	0.13	<0.01	0.10	0.054	0.09	0.098	0.09	0.088
Waist-to-hip ratio	0.05	0.255	0.08	0.107	0.10	0.055	0.08	0.151
Mean skin-fold thickness (cm)	0.12	<0.01	0.05	0.373	0.05	0.332	0.03	0.606
	Conventional DBP (mmHg)		24-h DBP (mmHg)		Daytime DBP (mmHg)		Night-time DBP (mmHg)	
Waist circumference (cm)	0.41	<0.0001	0.12	0.033	0.13	0.018	0.11	0.048
Body mass index (kg/m ²)	0.21	<0.0001	0.06	0.231	0.06	0.314	0.06	0.237
Waist-to-hip ratio	0.12	0.029	0.08	0.162	0.10	0.062	0.09	0.115
Mean skin-fold thickness (cm)	0.17	0.002	0.02	0.675	0.03	0.637	0.03	0.584

The P values indicated in bold are significant. ^aFrom stepwise regression analysis including indices of adiposity considered separately and age, gender, alcohol and tobacco intake, postmenopausal status (confirmed with follicle stimulating hormone measurements), the presence or absence of diabetes mellitus or inappropriate blood glucose control, and the use of antihypertensive therapy in the regression model.

Fig. 3



Partial correlation coefficients (r) and 95% confidence intervals for the relationship between indices of obesity and conventional (BPC) or 24-h (BP24) systolic and diastolic blood pressure after including all indices of adiposity together in the regression equation. Partial correlation coefficients are after adjustments for other confounders (see Table 3 for additional confounders) in the study group ($n = 300$, left panels) and in the subgroup not receiving antihypertensive therapy (untreated subjects, $n = 237$, right panels). BMI, body mass index; skin-fold, skin-fold thickness; WC, waist circumference; WHR, waist-to-hip ratio. P values are for significant independent relationships.

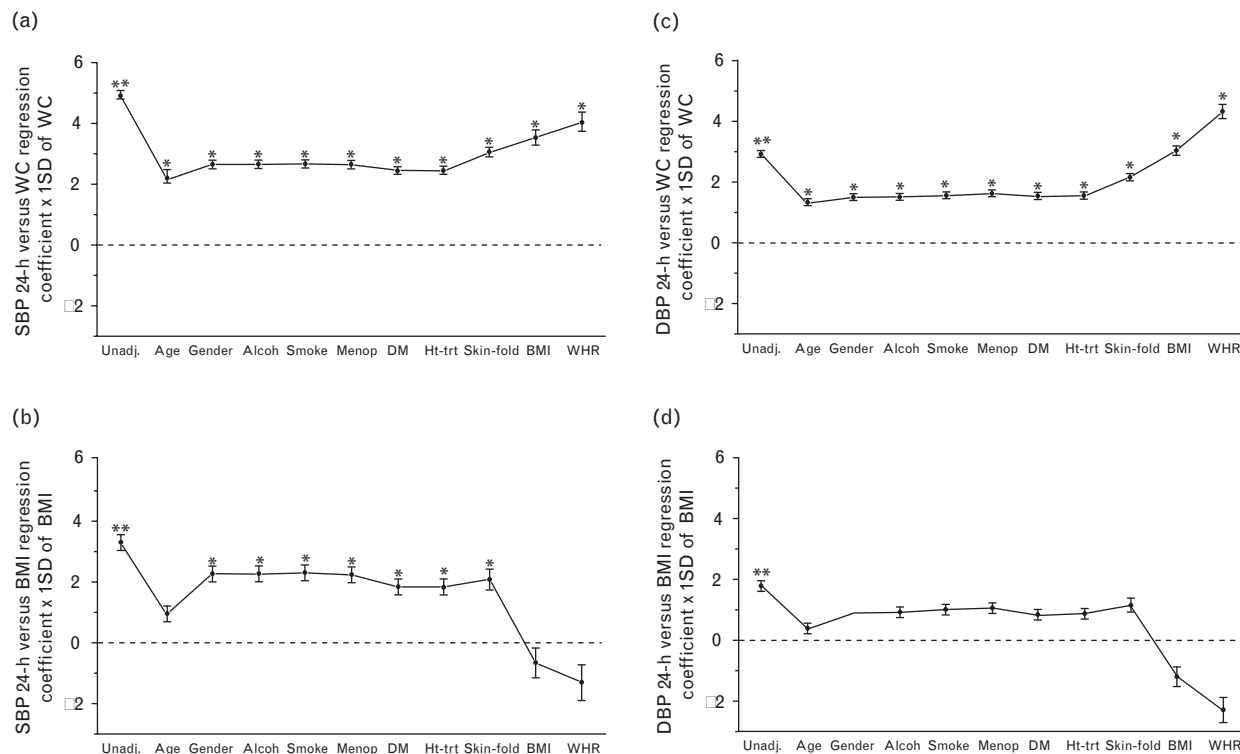
the model (Fig. 3, left panels). In contrast, neither BMI nor skin-fold thickness were significantly associated with clinic or 24-h BP after adjusting for WC and waist-to-hip ratio (Fig. 3, left panels). Similarly, in the subgroup of subjects not receiving antihypertensive therapy, WC was independently related to either conventional or 24-h BP after BMI, waist-to-hip ratio and skin-fold thickness were included in the model (Fig. 3, right panels). In contrast, neither BMI nor skin-fold thickness were significantly associated with either clinic or 24-h BP after adjusting for WC and waist-to-hip ratio (Fig. 3, right panels). In addition, the independent relationship between WC and either daytime or night-time BP persisted after BMI, waist-to-hip ratio and skin-fold thickness were included

in the model (in all subjects with ambulatory BP data the partial correlation coefficients for WC and daytime SBP were: $r = 0.16$, $P = 0.025$; daytime DBP: $r = 0.15$, $P = 0.009$; night-time SBP: $r = 0.10$, $P = 0.058$; night-time DBP: $r = 0.12$, $P = 0.027$; in subjects not receiving antihypertensive therapy, the partial correlation coefficients for WC and daytime SBP were: $r = 0.18$, $P = 0.002$; daytime DBP: $r = 0.14$, $P = 0.018$; night-time SBP: $r = 0.17$, $P = 0.005$; night-time DBP: $r = 0.14$, $P = 0.015$).

Predicted size effects of indexes of adiposity on ambulatory blood pressure

The size effects of WC on 24-h ambulatory systolic BP associated with a 15 cm (~ 1 SD) increase in WC were

Fig. 4



Unadjusted (unadj.) and adjusted differences in 24-h systolic (SBP) and diastolic (DBP) blood pressure associated with one standard deviation (SD) increase in waist circumference [WC – panels (a) and (c), SD ~15 cm] or body mass index [BMI – panels (b) and (d), SD ~7 kg/m²] in the study group ($n = 300$). Alcoh, alcohol intake; Smoke, tobacco intake; Menop, menopausal status; DM, presence or absence of diabetes mellitus or inappropriate blood glucose control; Ht-trl, hypertension treatment; Skin-fold, skin-fold thickness; WHR, waist-to-hip ratio. * $P < 0.05$, ** $P < 0.005$.

partially improved on after further adjusting for skin-fold thickness, waist-to-hip ratio and BMI (Fig. 4a). Before adjusting for BMI, waist-to-hip ratio and skin-fold thickness, every 1 SD (15 cm) increase in WC resulted in a 2.46 mmHg increase in 24-h systolic BP (Fig. 4a). In comparison, after adjusting for skin-fold thickness, BMI and waist-to-hip ratio, every 1 SD (15 cm) increase in WC resulted in a 4.04 mmHg increase in 24-h systolic BP (Fig. 4a). In contrast, the size effects of BMI on 24-h ambulatory systolic BP associated with a 7.4 kg/m² (~1 SD) increase in BMI were considerably reduced after adjusting for WC and waist-to-hip ratio (Fig. 4b). Similarly, before adjusting for BMI, waist-to-hip ratio and skin-fold thickness, every 1 SD (15 cm) increase in WC resulted in a 1.55 mmHg increase in 24-h diastolic BP (Fig. 4c); whereas, after adjusting for skin-fold thickness, BMI and waist-to-hip ratio, every 1 SD (15 cm) increase in WC resulted in a 4.33 mmHg increase in 24-h diastolic BP (Fig. 4c). In contrast, the size effects of BMI on 24-h ambulatory diastolic BP associated with a 7.4 kg/m² (~1 SD) increase in BMI were considerably reduced after adjusting for WC and waist-to-hip ratio (Fig. 4d).

The analyses in the subgroup not receiving antihypertensive therapy were similar, with every 1 SD (14.7 cm)

increase in WC resulting in 2.69 and 1.57 mmHg increases in 24-h systolic and diastolic BP, respectively, compared to increases of 4.74 and 4.62 mmHg in 24-h systolic and diastolic BP, respectively, after adjusting for BMI, waist-to-hip ratio and skin-fold thickness. In contrast, the effects of BMI on 24-h ambulatory systolic (1.96) and diastolic (0.98) BP associated with a 6.8 kg/m² (~1 SD) increase in BMI were considerably reduced after adjusting for WC and waist-to-hip ratio (–2.01 and –2.41 for systolic and diastolic BP, respectively).

Discussion

The main finding of the present study is that waist circumference is the only clinical index of adiposity that was associated with an increased ambulatory and conventional systolic and diastolic BP independent of other indices of adiposity.

A recent large study conducted in a European population, in which abdominal fat effects were not assessed, has demonstrated convincingly that BMI is associated with ambulatory BP [34]. The present study is the first conducted in a relatively large, randomly selected population sample that has explored whether the relationship between ambulatory BP and indices of central adiposity

(WC and waist-to-hip ratio) are independent of other indices of adiposity. In this regard, the relationship between WC and 24-h BP was independent of BMI and skin-fold thickness, whereas the relationship between BMI and 24-h BP was masked by adding WC to the regression equation. As ambulatory BP is a better index of cardiovascular outcomes [22–25] and target organ effects [26] than conventional BP values, these data support an important role for the use of WC when predicting the BP that is more closely associated with cardiovascular outcomes and target organ damage than conventional BP.

Prior studies conducted in small, non-random samples have explored whether waist-to-hip ratio is associated with ambulatory BP independent of BMI [17–21]. Some of these studies have suggested that waist-to-hip ratio is independently related to ambulatory BP in both adults ($n = 51$ –97) [17,18] and in 140 children [20], findings not supported by the present study. On the other hand, consistent with the results of the present study, some previous studies have demonstrated that waist-to-hip ratio is not independently associated with ambulatory systolic or diastolic BP in 156 schoolteachers [19] and 357 untreated hypertensives [21]. The lack of a consistent relationship between waist-to-hip ratio and ambulatory BP may be explained by the poor relationship between visceral fat mass and waist-to-hip ratio [35–39]. In this regard, some studies have highlighted the critical role of visceral fat mass in mediating BP changes [7–16].

Three possibilities may explain the independent relationship between WC, but not BMI with BP in the present and in previous [3,4] studies. First, an inconsistent relationship between BMI and adiposity may occur, particularly in populations of African descent [6]. Thus BMI may not be a reliable index of adipose tissue mass in some populations. Second, as visceral fat mass may be important in mediating BP changes [7–16], it is also possible that BMI is not that closely related to the fat compartment that contributes to BP; however, in the present study the correlation coefficient between WC and BMI was remarkably strong ($r = 0.84$). Third, the association between BMI and BP could be tempered by the presence of a genotype that moderates the relationship [40] or a genotype that increases the association between WC and BP.

The lack of an independent relationship between skin-fold thickness and BP in the present study may also be explained by the close relationship between visceral fat and BP [7–16]. Skin-fold thickness is an index of subcutaneous peripheral fat and, as indicated in the present study, has a poor correlation with indices of central fat. Interestingly, when indices of adiposity were considered separately in the regression model, skin-fold thickness and conventional systolic and diastolic BP were correlated, whereas skin-fold thickness and ambulatory BP were not. These data would suggest that although peripheral/

subcutaneous fat is associated with resting BP, it is not associated with ambulatory BP.

As compared to ambulatory BP, conventional BP is more likely to reflect an increase in sympathetic activity associated with the alerting reaction [41], and sympathetic overactivation has been shown to be associated with obesity [42]. Thus, the closer relationship between skin-fold thickness and conventional BP as compared to skin-fold thickness and ambulatory BP in the present study may be explained by an increase in sympathetic activity associated with the measurement of conventional BP (alerting reaction). Similarly, the closer relationship between WC and conventional diastolic BP as compared to WC and ambulatory diastolic BP in the present study may also be explained by an increase in sympathetic activity associated with the measurement of conventional BP.

The limitations of the present study include the cross-sectional design. Moreover, more direct measures of visceral fat (such as computed tomography) were not employed. However, the present study was not designed to determine the impact of visceral fat on ambulatory BP, but rather to identify which clinical index of adiposity is independently associated with ambulatory BP. The relatively lower proportion of males as compared to females recruited in the present study also raises the question as to whether the outcomes of the present study may only apply to females. The lower sample of males prevented us from performing gender-specific analysis with confidence in the outcomes; however, it is well recognized that obesity in males is more frequently accompanied by central rather than peripheral fat accumulation, hence the outcomes of the present study are unlikely to be through an effect noted only in females. As this study was performed in a population of African ancestry with a high prevalence of hypertension (42%) and a high proportion of subjects who were either overweight or obese (66%), these data may not be applicable to other populations with a different prevalence of hypertension or obesity.

In conclusion, the present study indicates that WC is the only clinical index of adiposity that is associated with ambulatory and conventional systolic and diastolic BP independent of other indices of adiposity. Therefore, the present data suggest that WC is the index of adiposity to use when assessing the impact of excess adiposity on ambulatory BP, a BP measurement that is more closely associated with cardiovascular outcomes than is conventional BP.

Acknowledgements

Nuclear families were recruited in the framework of the African Project on Genes in Hypertension, which was supported by the International Scientific and Technological Cooperation between South Africa and Flanders (contract number BIL 01/43), the Medical Research Council of

South Africa, the National Research Foundation of South Africa (Women in Research and the Thuthuka Programme), the Carnegie Foundation and the Circulatory Disorders Research Trust. The University Research Council of the University of the Witwatersrand also supported this work. This study would not have been possible without the voluntary collaboration of the participants. We are very grateful for the excellent technical assistance of Mthuthuzeli Kiviet, Nkele Maseko and Nomonde Molebatsi.

There are no conflicts of interest.

References

- Flegal KM, Carroll MD, Ogden CL, Johnson CL. Prevalence and trends in obesity among US adults, 1999–2000. *JAMA* 2002; **288**:1723–1727.
- Bourne LT, Lambert EV, Steyn K. Where does the black population of South Africa stand on the nutrition transition? *Public Health Nutr* 2002; **5**:157–162.
- Zhu S, Heymsfield SB, Toyoshima H, Wang Z, Pietrobello A, Heshka S. Race-ethnicity specific waist circumference cutoffs for identifying cardiovascular disease risk factors. *Am J Clin Nutr* 2005; **81**:409–415.
- Okosun IS, Cooper RS, Rotimi CN, Osotimehin B, Forrester T. Association of waist circumference with risk of hypertension and type 2 diabetes in Nigerians, Jamaicans and African Americans. *Diabetes Care* 1998; **21**:1836–1842.
- Harris MM, Stevens J, Thomas N, Schreiner P, Folsom AR. Associations of fat distribution and obesity with hypertension in a bi-ethnic population: The ARIC Study. *Obesity Res* 2000; **8**:516–524.
- Luke A, Durazo-Arvizu R, Rotimi C, Prewitt TE, Forrester T, Wilks R, et al. Relations between body mass index and body fat in black population samples from Nigeria, Jamaica, and the United States. *Am J Epidemiol* 1997; **45**:620–628.
- Williams PT, Fortmann SP, Terry RB, Garay SC, Vrazin KM, Ellsworth N, Wood PD. Associations of dietary fat, regional adiposity and blood pressure in men. *JAMA* 1987; **257**:3251–3256.
- Peiris AN, Sothmann MS, Hoffmann RG, Hennes MI, Wilson CR, Gustafson AB, Kissebah AH. Adiposity, fat distribution and cardiovascular risk. *Ann Intern Med* 1989; **110**:867–872.
- Kanai H, Matsuzawa Y, Kotani K, Keno Y, Kobatake T, Nagai Y, et al. Close correlation of intra-abdominal fat accumulation to hypertension in obese women. *Hypertension* 1990; **16**:484–490.
- Raison JM, Achimastos AM, Safar ME. Sex-dependence of body fat distribution in patients with obesity and hypertension. *Clin Exp Hypertens* 1992; **14**:505–525.
- Boyko EJ, Leonetti DL, Bergstrom RW, Newell-Morris L, Fujimoto WY. Visceral adiposity, fasting plasma insulin and blood pressure in Japanese-Americans. *Diabetes Care* 1995; **18**:174–181.
- Lerario AC, Bosco A, Rocha M, Santomaura AT, Luthold W, Giannella D, Wajchenberg BL. Risk factors in obese women, with particular reference to visceral fat component. *Diabetes Metab* 1997; **23**:68–74.
- Okosun IS, Prewitt TE, Cooper RS. Abdominal obesity in the United States: prevalence and attributable risk of hypertension. *J Hum Hypertens* 1999; **13**:425–430.
- Ho SC, Chen YM, Woo JL, Leung SS, Lam TH, Janus ED. Association between simple anthropometric indices and cardiovascular risk factors. *Int J Obes Relat Metab Disord* 2001; **25**:1689–1697.
- Hayashi T, Boyko EJ, Leonetti DL, McNeely MJ, Newell-Morris L, Kahn SE, Fujimoto WY. Visceral adiposity and the prevalence of hypertension in Japanese Americans. *Circulation* 2003; **108**:1718–1723.
- Ding J, Visser M, Kritchevsky AB, Nevitt M, Sutton-Tyrrell K, Harris TB. The association of regional fat depots with hypertension in older persons of white and African American ethnicity. *Am J Hypertens* 2004; **7**:971–976.
- Guagnano MT, Merlitti D, Murri R, Palliti VP, Sensei S. Ambulatory blood pressure monitoring in evaluating the relationship between obesity and blood pressure. *J Hum Hypertens* 1994; **8**:245–250.
- Guagnano MT, Ballone E, Merlitti D, Murri R, Pace-Palliti V, Pilotti R, Sensei S. Association between anthropometric and ultrasound measurements of fatness with ambulatory blood pressure monitoring in obese women. *Int J Obes Relat Metab Disord* 1997; **21**:632–636.
- Steptoe A, Cropley M, Griffith J, Joeckes K. The influence of abdominal obesity and chronic work stress on ambulatory blood pressure in men and women. *Int J Obes Relat Metab Disord* 1999; **23**:1184–1191.
- Lurbe E, Alvarez V, Liao Y, Tacons J, Cooper R, Cremades B, et al. The impact of obesity and body fat distribution on ambulatory blood pressure in children and adolescents. *Am J Hypertens* 1998; **11**:418–424.
- Feldstein CA, Akopian M, Olivieri AO, Krmer AP, Nasi M, Garrido D. A comparison of body mass index and waist-to-hip ratio as indicators of hypertension risk in an urban Argentine population: A hospital study. *Nutr Metab Cardiovasc Dis* 2005; **15**:310–315.
- Verdecchia P, Porcellati C, Schillaci G, Borgioni C, Ciucci A, Battistelli M, et al. Ambulatory blood pressure. An independent predictor of prognosis in essential hypertension. *Hypertension* 1994; **24**:793–801.
- Clement DL, De Buyzere ML, De Bacquer DA, de Leeuw PW, DuPrez DA, Fagard RH, et al. Office versus ambulatory pressure study investigators. Prognostic value of ambulatory blood-pressure recordings in patients with treated hypertension. *N Engl J Med* 2003; **348**:2407–2415.
- Staessen JA, Thijs L, Fagard R, O'Brien ET, Clement D, de Leeuw PW, et al. Predicting cardiovascular risk using conventional versus ambulatory blood pressure in older patients with systolic hypertension. Systolic Hypertension in Europe Trial Investigators. *JAMA* 1999; **282**:539–546.
- Okhubo T, Imai Y, Tsuji I, Nagai K, Ito S, Satoh H, Hisamichi S. Reference values for 24-h ambulatory blood pressure monitoring based on prognostic criteria: the Ohasama Study. *Hypertension* 1998; **32**:255–259.
- Mancia G, Parati G. Ambulatory blood pressure monitoring and organ damage. *Hypertension* 2000; **36**:894–900.
- Shiburi CP, Staessen JA, Maseko M, Wojciechowska W, Thijs L, van Bortel LM, et al. Reference values for Sphygmocor measurements in South Africans of African ancestry. *Am J Hypertens* 2006; **19**:40–46.
- Peters AL, Davidson MB, Schriger DL, Hasselblad V. A clinical approach for the diagnosis of diabetes mellitus: an analysis using glycosylated hemoglobin levels. Meta-analysis Research Group on the Diagnosis of Diabetes Using Glycated Hemoglobin Levels. *JAMA* 1996; **276**:1246–1252.
- Maseko MJ, Majane HO, Milne J, Norton GR, Woodiwiss AJ. Salt intake in an urban, developing South African community. *Cardiovasc J South Afr* 2006; **17**:186–191.
- Staessen J, Bulpitt CJ, Fagard R, Joossens JV, Lijnen P, Amery A. Salt intake and blood pressure in the general population: a controlled intervention trial in two towns. *J Hypertens* 1988; **6**:965–973.
- O'Brien E, Asmar R, Beilin L, Imai Y, Mallion JM, Mancia G, et al., European Society of Hypertension Working Group on Blood Pressure Monitoring. European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. *J Hypertens* 2003; **21**:821–848.
- Thijs L, Staessen J, Fagard R. Analysis of the diurnal blood pressure curve. *High Blood Press Cardiovasc Prev* 1992; **1**:17–28.
- Fagard RH, Staessen JA, Thijs L. Optimal definition of daytime and night-time blood pressure. *Blood Press Monit* 1997; **2**:315–321.
- Kotsis V, Stabouli S, Boulidin M, Low SA, Toumanidis S, Zakopoulos N. Impact of obesity on 24-h ambulatory blood pressure and hypertension. *Hypertension* 2005; **45**:602–607.
- Kvist H, Chowhury B, Grangard U, Tylen U, Sjostrom L. Total and visceral adipose tissue volumes derived from measurements with computed tomography in adult men and women: predictive equations. *Am J Clin Nutr* 1988; **48**:1351–1361.
- Seidell JC, Ossterlee A, Deurenberg P, Hautvast JG, Ruijs JH. Abdominal fat deposits measured with computer tomography: effects of degree of obesity, sex, and age. *Eur J Clin Nutr* 1988; **42**:805–815.
- Pouliot MC, Despres JP, Lemeux S, Moorjani S, Bouchard C, Tremblay A, et al. Waist circumference and abdominal sagittal diameter: best simple anthropometric index of abdominal visceral adipose tissue accumulation and related cardiovascular risk in men and women. *Am J Cardiol* 1994; **73**:460–468.
- Wajchenberg BL. Subcutaneous and visceral adipose tissue: their relation to the metabolic syndrome. *Endocrine Reviews* 2000; **21**:697–738.
- Stewart KJ, DeRegis JR, Turner KL, Bacher AC, Sung J, Hees PS, et al. Usefulness of anthropometrics and dual energy X-ray absorptiometry for estimating abdominal obesity measured by magnetic resonance imaging in older men and women. *J Cardiopulm Rehab* 2003; **23**:109–114.
- Tiago AD, Samani NJ, Candy GP, Brooksbank R, Libhaber EN, Sareli P, et al. Angiotensinogen gene promoter region variant modifies body size—ambulatory blood pressure relations in hypertension. *Circulation* 2003; **106**:1483–1487.
- Weber MA, Neutel JM, Smith DHG, Graettinger WF. Diagnosis of mild hypertension by ambulatory blood pressure monitoring. *Circulation* 1994; **90**:2291–2298.
- Tentolouris N, Liatis S, Katsilambros N. Part II. Central stress activity and peripheral tissue sensitivity in the genesis of obesity and the metabolic syndrome: sympathetic system activity in obesity and metabolic syndrome. *Ann NY Acad Sci* 2006; **1083**:1289–1252.